

Order information

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
08058750190	Uric Acid ver.2 (1300 tests)	System-ID 2117 001 cobas c 303, cobas c 503
10759350360	Calibrator f.a.s. (12 x 3 mL)	Code 20401
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001

English

For use in the USA only

System information

UA2: ACN 21170 (Serum/plasma)

UA2U: ACN 21171 (Urine)

Intended use

In vitro test for the quantitative determination of uric acid in human serum, plasma and urine on Roche/Hitachi **cobas c** systems.

Summary^{1,2,3,4,5,6,7,8,9,10,11,12,13,14}

Uric acid is the final product of purine metabolism in the human organism. Uric acid measurements are used in the diagnosis and treatment of numerous renal and metabolic disorders, including renal failure, gout, leukemia, psoriasis, starvation or other wasting conditions, and of patients receiving cytotoxic drugs.

The oxidation of uric acid provides the basis for two approaches to the quantitative determination of this purine metabolite. One approach is the reduction of phosphotungstic acid in an alkaline solution to tungsten blue, which is measured photometrically. The method is, however, subject to interferences from drugs and reducing substances other than uric acid.

A second approach, described by Praetorius and Poulsen, utilizes the enzyme uricase to oxidize uric acid; this method eliminates the interferences intrinsic to chemical oxidation. Uricase can be employed in methods that involve the UV measurement of the consumption of uric acid or in combination with other enzymes to provide a colorimetric assay.

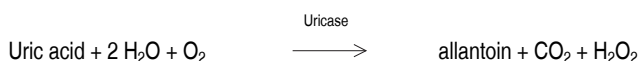
Another method is the colorimetric method developed by Town et al. The sample is initially incubated with a reagent mixture containing ascorbate oxidase and a clearing system. In this test system it is important that any ascorbic acid present in the sample is eliminated in the preliminary reaction; this precludes any ascorbic acid interference with the subsequent POD indicator reaction. Upon addition of the starter reagent, oxidation of uric acid by uricase begins.

The Roche assay described here is a slight modification of the colorimetric method described above. In this reaction, the peroxide reacts in the presence of peroxidase (POD), N-ethyl-N-(2-hydroxy-3-sulfoethyl)-3-methylaniline (TOOS), and 4-aminophenazone to form a quinone-diimine dye. The intensity of the red color formed is proportional to the uric acid concentration and is determined photometrically.

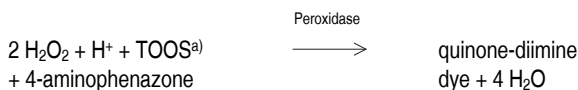
Test principle

Enzymatic colorimetric test.

Uricase cleaves uric acid to form allantoin and hydrogen peroxide.



In the presence of peroxidase, 4-aminophenazone is oxidized by hydrogen peroxide to a quinone-diimine dye.



a) N-ethyl-N-(2-hydroxy-3-sulfoethyl)-3-methylaniline

The color intensity of the quinone-diimine formed is directly proportional to the uric acid concentration and is determined by measuring the increase in absorbance.

Reagents - working solutions

- R1** Phosphate buffer: 0.05 mol/L, pH 7.8; TOOS: 7 mmol/L; fatty alcohol polyglycol ether: 4.8 %; ascorbate oxidase (EC 1.10.3.3; zucchini) ≥ 83.5 µkat/L (25 °C); stabilizers; preservative
- R3** Phosphate buffer: 0.1 mol/L, pH 7.8; potassium hexacyanoferrate (II): 0.3 mmol/L; 4-aminophenazone ≥ 3 mmol/L; uricase (EC 1.7.3.3; Arthrobacter protophormiae) ≥ 83.4 µkat/L (25 °C); peroxidase (POD) (EC 1.11.1.7; horseradish) ≥ 50 µkat/L (25 °C); stabilizers; preservative

R1 is in position B and R3 is in position C.

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.



Warning

H319 Causes serious eye irritation.

H411 Toxic to aquatic life with long lasting effects.

Prevention:

P264 Wash hands thoroughly after handling.

P273 Avoid release to the environment.

P280 Wear eye protection/ face protection.

Response:

P337 + P313 If eye irritation persists: Get medical advice/attention.

P391 Collect spillage.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C:

See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer:

26 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum.

Plasma: Li-heparin and K₂-EDTA plasma.

EDTA plasma values are approximately 7 % lower than serum values.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Urine: Assay urinary uric acid as soon as possible. Do not refrigerate.

To prevent ureate precipitation in urine samples, add sodium hydroxide to keep urine alkaline (pH > 8.0). To achieve stated uric acid stability, add NaOH prior to sample collection. Urine samples are diluted 1 + 10 with distilled/deionized water or 0.9 % NaCl. This dilution is taken into account in the calculation of the results. If stabilizers are added to the sample, the sample index feature must not be used.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability in serum/plasma: ¹⁵	7 days at 4-8 °C
	3 days at 20-25 °C
	6 months at -20 °C

Stability in urine ¹⁵ (upon NaOH addition):	4 days at 20-25 °C
--	--------------------

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

See "Order information" section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma**Test definition**

Reporting time	10 min		
Wavelength (sub/main)	700/546 nm		
Reagent pipetting		Diluent (H ₂ O)	
R1	55 µL		19 µL
R3	11 µL		15 µL
Sample volumes	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	2.3 µL	–	–
Decreased	3.6 µL	21 µL	61 µL

Increased	2.3 µL	–	–
-----------	--------	---	---

Application for urine**Test definition**

Reporting time	10 min		
Wavelength (sub/main)	700/546 nm		
Reagent pipetting		Diluent (H ₂ O)	
R1	55 µL		19 µL
R3	11 µL		15 µL
Sample volumes	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	2.3 µL	10 µL	100 µL
Decreased	2.3 µL	4 µL	106 µL
Increased	2.3 µL	10 µL	100 µL

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration**Application for serum/plasma (ACN 21170)**

Calibrators	S1: H ₂ O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	Automatic full calibration
	- after reagent lot changed
	Full calibration
	- after 12 weeks on-board
	- as required following quality control procedures

Application for urine (ACN 21171)

Transfer of calibration from serum/plasma application (ACN 21170)

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against ID/MS.¹⁶

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

Serum/plasma:	PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2
Urine:	Quantitative urine controls are recommended for routine quality control.

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte concentration of each sample in the unit mg/dL (µmol/L, mg/L, mmol/L).

Conversion factors:	mg/dL x 59.5 = µmol/L
	mg/dL x 10.0 = mg/L
	mg/dL x 0.0595 = mmol/L

Limitations - interference

Criterion: Recovery within $\pm 10\%$ of initial value at a uric acid concentration of 7 mg/dL (417 $\mu\text{mol/L}$).

Serum/plasma

Icterus:¹⁷ No significant interference up to an I index of 40 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 684 $\mu\text{mol/L}$ or 40 mg/dL).

Hemolysis:¹⁷ No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 $\mu\text{mol/L}$ or 1000 mg/dL).

Lipemia (Intralipid):¹⁷ No significant interference up to an L index of 1500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 0.17 mmol/L (3 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.^{18,19} Exceptions: Calcium dobesilate causes artificially low uric acid results.

Uricase reacts specifically with uric acid. Other purine derivatives can inhibit the uric acid reaction.

Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.²⁰

Acetaminophen intoxications are frequently treated with N-Acetylcysteine. N-Acetylcysteine at the therapeutic concentration when used as an antidote and the Acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low results.

Venipuncture should be performed prior to the administration of Metamizole. Venipuncture immediately after or during the administration of Metamizole may lead to falsely low results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.²¹

Urine

Drugs: No interference was found at therapeutic concentrations using common drug panels.¹⁹ Exceptions: Calcium dobesilate, Levodopa and methyl dopa can all cause artificially low uric acid results.

High homogentisic acid concentrations in urine samples lead to false results.

Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.

Acetaminophen, Acetylcysteine and Metamizole are metabolized quickly. Therefore, interference from these substances is unlikely but cannot be excluded.

Hemolysis: No significant interference up to an H index of 750 (approximate hemoglobin concentration: 466 $\mu\text{mol/L}$ or 750 mg/dL).

Urea: No significant interference from urea up to a concentration of 2100 mmol/L (12612 mg/dL).

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions refer to the operator's manual.

Limits and ranges**Measuring range***Serum/plasma*

0.2-25 mg/dL (11.9-1487 $\mu\text{mol/L}$)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

Urine

2.2-275 mg/dL (131-16362 $\mu\text{mol/L}$)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

Lower limits of measurement*Limit of Blank, Limit of Detection and Limit of Quantitation**Serum/plasma*

Limit of Blank = 0.2 mg/dL

Limit of Detection = 0.2 mg/dL

Limit of Quantitation = 0.2 mg/dL

Urine

Limit of Blank = 2.2 mg/dL

Limit of Detection = 2.2 mg/dL

Limit of Quantitation = 2.2 mg/dL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from $n \geq 60$ measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration uric acid samples.

Expected values**mg/dL***Serum/plasma*²²

Males: 3.4-7.0 mg/dL

Females: 2.4-5.7 mg/dL

Urine (reference range according to Krieg and Colombo)

1st morning urine²³ 37-92 mg/dL*

24-hour urine²⁴ 200-1000 mg/day*

corresponding to 13-67 mg/dL

(calculated from a urine volume of 1.5 L/24 h)

 $\mu\text{mol/L}$ *Serum/plasma*²²

Males: 202.3-416.5 $\mu\text{mol/L}$ *

Females: 142.8-339.2 $\mu\text{mol/L}$ *

* calculated by unit conversion factor

Urine (reference range according to Krieg and Colombo)

1st morning urine²³ 2200-5475 $\mu\text{mol/L}$

24-hour urine²⁴ 1200-5900 $\mu\text{mol/day}$

corresponding to 773-3986 $\mu\text{mol/L}$

(calculated from a urine volume of 1.5 L/24 h)

Urine (reference range according to Tietz)²⁵

Average diet 250-750 mg/24 hours

Low purine diet
Females < 400 mg/24 hours

Males	< 480 mg/24 hours
High purine diet	< 1000 mg/24 hours

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogeneous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c 503** analyzer.

Serum/plasma

Repeatability	Mean mg/dL	SD mg/dL	CV %
PCCC1 ^{b)}	4.60	0.0193	0.4
PCCC2 ^{c)}	10.6	0.0655	0.6
Human serum 1	0.430	0.00713	1.7
Human serum 2	2.32	0.0147	0.6
Human serum 3	6.66	0.0347	0.5
Human serum 4	12.0	0.0756	0.6
Human serum 5	21.4	0.129	0.6

Intermediate precision	Mean mg/dL	SD mg/dL	CV %
PCCC1 ^{b)}	4.60	0.0467	1.0
PCCC2 ^{c)}	10.6	0.0983	0.9
Human serum 1	0.430	0.00880	2.0
Human serum 2	2.32	0.0185	0.8
Human serum 3	6.66	0.0400	0.6
Human serum 4	12.0	0.0940	0.8
Human serum 5	21.4	0.143	0.7

b) PreciControl ClinChem Multi 1

c) PreciControl ClinChem Multi 2

Urine

Repeatability	Mean mg/dL	SD mg/dL	CV %
Control 1 ^{d)}	9.05	0.0780	0.9
Control 2 ^{d)}	16.1	0.0957	0.6
Human urine 1	2.91	0.0584	2.0
Human urine 2	37.1	0.171	0.5
Human urine 3	74.7	0.279	0.4
Human urine 4	115	0.556	0.5
Human urine 5	224	0.866	0.4

Intermediate precision	Mean mg/dL	SD mg/dL	CV %
Control 1 ^{d)}	9.18	0.144	1.6

Control 2 ^{d)}	16.1	0.159	1.0
Human urine 1	3.06	0.576	18.8
Human urine 2	37.1	0.615	1.7
Human urine 3	74.9	1.93	2.6
Human urine 4	115	4.34	3.8
Human urine 5	224	1.39	0.6

d) commercially available control material

Method comparison

Uric acid values for human serum, plasma and urine obtained on a **cobas c 503** analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c 501** analyzer (x).

Serum/plasma

Sample size (n) = 88

Passing/Bablok ²⁶	Linear regression
$y = 1.004x - 0.0207 \text{ mg/dL}$	$y = 1.008x - 0.0265 \text{ mg/dL}$
$r = 0.985$	$r = 1.000$

The sample concentrations were between 0.290 and 24.6 mg/dL.

Urine

Sample size (n) = 81

Passing/Bablok ²⁶	Linear regression
$y = 1.002x - 0.168 \text{ mg/dL}$	$y = 1.004x - 0.162 \text{ mg/dL}$
$r = 0.987$	$r = 1.000$

The sample concentrations were between 3.27 and 270 mg/dL.

Uric acid values for human serum, plasma and urine obtained on a **cobas c 303** analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c 501** analyzer (x).

Serum/plasma

Sample size (n) = 83

Passing/Bablok ²⁶	Linear regression
$y = 1.000x + 0.003 \text{ mg/dL}$	$y = 1.023x - 0.141 \text{ mg/dL}$
$r = 0.979$	$r = 0.998$

The sample concentrations were between 0.200 and 23.7 mg/dL.

Urine

Sample size (n) = 102

Passing/Bablok ²⁶	Linear regression
$y = 1.038x - 0.0408 \text{ mg/dL}$	$y = 1.057x - 0.990 \text{ mg/dL}$
$r = 0.991$	$r = 1.000$

The sample concentrations were between 2.45 and 243 mg/dL.

References

- Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995.
- Keller H, ed. Klinisch-chemische Labordiagnostik für die Praxis, 2nd ed. Stuttgart/New York: Georg Thieme Verlag 1991.
- Rice EW, Grogan BS. 1960 survey of clinical chemistry procedures used by members of the American Association of Clinical Chemists. Clin Chem 1962;8:181-193.
- Kageyama N. A direct colorimetric determination of uric acid in serum and urine with uricase-catalase system Clin Chim Acta 1971;31:421-426.
- DiGiorgio J, Henry RJ, et al. eds. Clinical Chemistry: Principles and Technics. 2nd ed. New York, NY: Harper and Row 1974:532.
- Kaiser E, et al. Wiener Klin Wschr 1972;84:217.
- Kim EK, Waddel LD, Sunderland MLE, et al. Observations on Diagnostic Kits for the Determination of Uric Acid. Clin Biochem 1971;4:279-286.

- 8 Elking MP, Karat HF. Drug induced modifications of laboratory test values. Am J Hosp Pharm 1968;25(9):484-519.
- 9 Young DS, Thomas DW, Friedman RB, et al. Effects of drugs on clinical laboratory tests. Clin Chem 1972;18(10):1041.
- 10 Küffer H. Causes of misleading laboratory results: disturbances due to drugs. Therap Umschau 1971;28(10):669-680.
- 11 Haug HG. Diagnostik 1972;5:85.
- 12 Singh HP, Hebert MA, Gault MH. Effect of Some Drugs on Clinical Laboratory Values as Determined by the Technicon SMA 12-60. Clin Chem 1972;18(2):137-144.
- 13 Praetorius E, Poulsen H. Enzymatic determination of uric acid; with detailed directions. Scand J Clin Lab Invest 1953;5(3):273-280.
- 14 Town MH, Gehm S, Hammer B, et al. A sensitive colorimetric method for the enzymatic determination of uric acid. J Clin Chem Clin Biochem 1985;23:591.
- 15 WHO Publication: Use of anticoagulants in diagnostic laboratory investigations, WHO/DIL/LAB/99.1 Rev.2:Jan 2002.
- 16 Siekmann L. Determination of uric acid in human serum by isotope dilution-mass spectrometry. J Clin Chem Clin Biochem 1985;23:129-135.
- 17 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.
- 18 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.
- 19 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.
- 20 Dastych M, Wiewiorka O, Benovska M. Ethamsylate (Dicynone) Interference in Determination of Serum Creatinine, Uric Acid, Triglycerides, and Cholesterol in Assays Involving the Trinder Reaction; In Vivo and In Vitro. Clin Lab 2014;60:1373-1376.
- 21 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.
- 22 Thefeld W, Hoffmeister H, Busch EW, et al. Normalwerte der Serumharnsäure in Abhängigkeit von Alter und Geschlecht mit einem neuen enzymatischen Harnsäurefarbstest. Dtsch Med Wschr 1973;98:380-384.
- 23 Krieg M, Gunsser KJ, Steinhagen-Thiessen E, et al. Vergleichende quantitative Analytik klinisch-chemischer Kenngrößen im 24-Stunden-Urin und Morgenurin. J Clin Chem Clin Biochem 1986 Nov;24(11):863-869.
- 24 Colombo JP, ed. Klinisch-chemische Urindiagnostik. Rotkreuz: LABOLIFE-Verlagsgemeinschaft 1994:180.
- 25 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests, 4th edition. St. Louis (MO): Saunders Elsevier 2006;1098-1100.
- 26 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT

Contents of kit



Volume for reconstitution

GTIN

Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

COBAS, COBAS C and PRECICONTROL are trademarks of Roche.

All other product names and trademarks are the property of their respective owners.

Additions, deletions or changes are indicated by a change bar in the margin.

© 2021, Roche Diagnostics



Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

